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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,195	12/19/2001	David Berd	1225/1D414US2	8483

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	
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07/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/025,195	BERD, DAVID	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,6 and 9-22* is/are pending in the application.

4a) Of the above claim(s) *3 and 9-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 6 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of the application has changed. This case has now been transferred as of 6/20/2007. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Brandon Fetterolf, Group Art Unit 1642.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/30/2007 has been entered.

Claims 2-3, 6 and 9-22 are pending

Claims 3 and 9-21 are withdrawn from consideration.

Claims 2, 6 and 22 are currently under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 6 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al. (WO 96/40173, 1996, IDS) in view of Sensi et al. (J. Clin. Invest. 1997; 99: 710-717).

Berd et al. teach a method of treating cancer comprising administering cyclophosphamide followed by administering a therapeutically effective amount of a composition comprising a tumor cell or tumor cell extract, wherein the composition is injected ever 4 weeks for a total of eight treatments (page 23, lines 3-9 and lines 23-28). With regards to the cancer, the WO document teaches that cancers treatable with the compositions include, but are not limited to, colon cancer (page 16, line 2). With regards to the tumor cells, the WO document teaches that the tumor cells

originate from the type of cancer which is to be treated and include, haptenized, irradiated autologous tumor cells (page 16, lines 15-16, page 18, lines 1-4 and 24-26). With regards to the hapten, the WO document teaches that the haptens include but are not limited to, DNP (page 23, lines 11-14). With regards to the cyclophosphamide, the WO document teaches that cyclophosphamide is administered 3 days prior to each vaccine administration to augment the immune response to the tumor cells, but does not have to given to patients considered to be deriving benefit from the therapy receiving subsequent vaccines, e.g., a composition comprising haptenized, irradiated autologous tumor cells (page 23, lines 6-10 and page 30, lines 2-5). Moreover, the WO document teaches that the compositions further comprise adjuvants including, but not limited to, *Bacillus Calmette-Guerin* (BCG). The WO document further teaches that the method additionally comprises administering a biological modifier such as IL-12 which causes the T-lymphocytes within the tumor mass to proliferate and become more active.

Berd et al. does not explicitly teach that the method consists of a single dose of cyclophosphamide prior the administration of repeated cycles of vaccine.

Sensi et al. teach a method of treating a patient having metastatic melanoma, comprising administering to the patient a low dose amount of cyclophosphamide followed by administration of irradiated, DNP-modified melanoma cells mixed with BCG adjuvant, wherein two administration schedules where tested: (a) DNP-vaccine administered every 28 days with cyclophosphamide administered 3 days before the first two vaccine injection (patient ED) and (b) DNP vaccine administered weekly for 6 wk with cyclophosphamide given 3 days before the 6-wk series (patients FC, CB, JB, RS, LC)(page 711, 1st column, 1st full paragraph). In particular, the reference teaches that the multiple lung metastases of patient JC, whom received DNP vaccine administered weekly for 6 wk with cyclophosphamide given 3 days before the 6-wk series, underwent >90% regression and survived from 35 months (page 711, 1st column, 2nd full paragraph). In contrast, the reference teaches that patient ED, whom received DNP-vaccine administered every 28 days with cyclophosphamide administered 3 days before the first two vaccine injection, had a mixed response (regression of some subcutaneous tumors simultaneously with growth of others.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of the references so as to modify the method taught by Berd et al. so as to administer a single dose of cyclophosphamide in view of the teachings of Sensi et

al. One would have been motivated to do so because Sensi et al. teach that patients showed a therapeutic benefit from receiving a single dose of cyclophosphamide 3 days prior to a a s wk administration of DNP-vaccine. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the method taught by Berd et al. so as to administer a single dose of cyclophosphamide in view of the teachings of Sensi et al., one would achieve a method for treating colon cancer.

Claims 2, 6 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoover et al. (Cancer, 1985: 55: 1236-1243, of record) in view of Berd et al. (US 5,290,551, 1994, of record).

Hoover et al. teach a successful method of active-specific immunotherapy of human colon cancer with an irradiated autologous colon tumor cell/bacillus calmette-Guerin vaccine (BCG) (abstract and table 1, page. 1240), wherein the method produced significant improvement in both disease-free status and survival of the immunized patients compared to unimmunized controls (see Fig. 2, p. 1240 and col. 2, page 1250). In particular, Hoover et al. teach repeated administration of the vaccine for two weeks (page 1238, 2nd column, 2nd full paragraph).

Hoover et al. does not explicitly teach that the irradiated tumor cells were irradiated or that a single dose of cyclophosphamide was administered prior to the repeated administration of the vaccine. Nor does Hoover et al. teach that the method further comprises eliciting T-lymphocytes infiltrating said colon carcinoma.

Berd et al. teach a method of treating patients/human melanoma patients with irradiated DNP autologous human melanoma cells mixed with BCG preceded by the low dose cyclophosphamide (CY) (abstract and claim 2). With regards to the cyclophosphamide, the patent teaches that cyclophosphamide is administered 3 days prior to each vaccine administration to augment the immune response to the tumor cells, but does not have to be given to patients considered to be deriving benefit from the therapy receiving subsequent vaccines (column 3, lines 33-36 and column 4, lines 36-39). Moreover, the patent teaches that toxicity of the therapy was limited to a local inflammatory response at the injection site and mild nausea and vomiting following CY (column 4, line 67 to column 5, line 1). In addition, the patent teaches that most tumor immunologist agree that getting T lymphocytes into the tumor mass is a prerequisite for tumor destruction by the immune system and that the efficacy of the instant vaccine process for the

treatment of cancer has been increased by immunizing with tumor cells conjugated to DNP (column 2, lines 44-48 and column 3, lines 12-15), wherein infiltration of T lymphocytes into the tumor mass is observed. As such, the patent teaches that this approach, which increases the number and capacity of lymphocytes entering the tumor is a significant advance in the art (column 3, line 68 to column 4, line 3).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of the references so as to modify the method taught by Hoover et al. so as to haptenize the irradiated autologous colon carcinoma cells in view of the teachings of Berd et al.. One would have been motivated to do so because Berd et al. specially teach that haptenization of tumor cells with DNP increase the efficiency of the vaccine process, wherein infiltration of T lymphocytes into the tumor mass is observed; and this approach, which increases the number and capacity of lymphocytes entering the tumor, is a significant advance int eh art. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the method taught by Hoover et al. so as to haptenize the irradiated autologous colon carcinoma cells in view of the teachings of Berd et al., one would achieve a method for treating colon carcinoma.

Secondly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer a single dose of cyclophosphamide as taught by Berd et a. in the method taught by Hoover et al. in view of Berd et al.. One would have been motivated to do so because Berd et al. teaches that while the the method taught by Hoover et al. so as to haptenize the irradiated autologous colon carcinoma cells in view of the teachings of Berd et al.. One would have been motivated to do so because Berd et al. teach that one the toxicities of the instant method is mild nausea and vomiting following CY administration; and further, that cyclophosphamide does not have to be given to patients considered to be deriving benefit from the therapy receiving subsequent vaccines. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering a single dose of cyclophosphamide, one would achieve a method of treating colon carcinoma while decreasing the toxicity associated with cyclophosphamide administration.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

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